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DESIGN SYNTHESIS AND BIOLOGICAL EVALUATION OF 1,2,4- TRIAZOLE AS AN ANTIMICROBIAL AGENT

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Abstract : New compounds were synthesized containing 1,2,4-triazole derivatives and tested for their antibacterial activity against gram positive and gram positive strains. A series of N-(3-(4-fluorophenyl)-5-mercaptp-4H-1,2,4-triazole-4-yl)-2-(substituted amines)acetamide were synthesized by esterification of 4- fluorobenzoic acid and further cyclization of hydrazide which is followed by reaction of carbon – di -sulfide and potassium hydrozide with the formation of intermediate potassium salt. The triazole prepared was subjected to N-acetylation with the treatment of choro acetyl chloride and formed the acetamide. The obtained nucleus was subjected to form different substituted derivatives with the treatment of 5 different secondary amines. The compounds were synthesized by conventional method and the stuctures of newly synthesized compounds were characterized by performing various physical as spectral techniques. This involves TLC, M.P , UV spectroscopy , FTIR and NMR spectroscopy . the antibacterial assay was performed for all the synthesized compounds by well diffusion method. The antibacterial screening reveals that the compound N-(3-(4-fluoro[phenyl)-5-mercapto-4H-1,2,4-triazole-4-yl)-2-((4-fluorophenyl)amino)acetamide (SA-03) was showed more promised and significant zone of incubation against *Bacillus Subtilis* and *Pseudomonas aeruginosa* ad show moderate activity as that of Standard Ofloxacin and Gentamycin against gram positive and gram negative bacteria .

***Index Terms* – 1,2,4-Triazole , Hydrazine hydrate , antimicrobial agent , antibacterial activity.**

INTRODUCTION

In today's era the most prescribed drug are the antibiotic drugs. Due to increased use of several antibiotic drug , may lives have ee saved. Although many antibiotics are available in the market , still there is the need of drug with higher activity and simultaneously lesser side effects [1] . A wide variety of heterocyclic system have been explored in order to develop pharmaceutically important molecule . Nitrogen – containing heterocycles are found in many medicines. Heterocyclic chemistry is most challenging and amply rewarding field , and by far heterocycles are the largest class in organic chemistry . A majority of pharmaceuticals , biologically active agrochemicals , additives and modifiers used in industrial applications are heterocyclic by nature . Synthetic organic chemistry make significant progress discovering and developing wide range of heterocyclic compounds for the benefit of mankind. One remarkable stuctural feature and characteristic to heterocycles, which continue to be exploited, is their capability to accommodate the constituent around a central frame . Among the heterocyclic compounds, triazole are one of the most key heterocycles exhibiting remarkable pharmacological activity as they are an essential constituent of all cells and living matter[2] .
1,2,4- Triazole moiety can influence lipophilicity , polarity and hydrogen bonding capacity of molecule, improving pharmacological , pharmacokinetic , toxicological , and physicochemical properties of the compounds. Triazole are heterocycle;ic compound featuring five membered rig with two carbon atom and three nitrogen atoms as part of the aromatic five membered ring . Triazole is an N- bridged aromatic heterocyclic compound that receive a considerable attention in recent years due to its biological activities . The name "Triazole" was first use by Bladin in 1855 for describing carbon- Nitrogen ring system $C_2H_3N_3$.[3] It is a white to pale yellow crystalline solid with weak , characteristic odour , soluble in water and alcohol , melts at 120 ℃ and boils at 260℃.[4] All the atoms in 1,2,4- triazole are sp^2 hybridized and have 6π electrons delocalized over the ring, responsible for its aromatic character . It is also known as s-triazole (symmetrical) . 1,2,4-triazole exists in two tautoimeric forms known as 1*H*-1,2,4-triazole and 4*H* – 1,2,4- triazole and it is very difficult to separate them due to their rapid interconversion [4].

NEED OF THE STUDY.

At present time, our medical field is suffering from the problem of antimicrobial resistance towards many microbial strains. Hence as prioritized by various health organizations, there is a need for the discovery or development of novel antimicrobial compounds

possessing a broad-spectrum activity exhibiting high effectiveness against those highly resistant Gram positive, Gram negative bacterial and fungal strains[5]. The antimicrobial agents available now have various drawbacks such as toxicity, drug resistance to microbes, and narrow spectrum of activity. Hence the design of new compounds to deal with these problems has become one of the most challenging targets in antibacterial and antifungal research today[6].

Many clinically important bacterial isolates still present a real challenge for many physicians, especially among those isolates that are highly resistant to current antibacterial agents and associated with serious and life-threatening infections. As consequence, a combination therapy of two or three antimicrobial agents has been sometimes practiced by physicians, especially in patients infected with highly resistant pathogenic bacteria. However, a great concern to the usage of combination therapy has been recently increased due to risks of side effects of drug reactions and interactions with other drugs administered to those type of patients. Therefore, the need for new class of compounds possessing a broad spectrum of antibacterial activity that are highly effective against those highly resistant Gram positive and negative bacteria is increasing, and it is becoming the top priority of most government heath institutions and the world health organizations[7].

The 1,2,4-triazole nucleus is stable to metabolic degradation and shows target specificity and wide spectrum of activities. The triazole ring contains three nitrogen atoms and can act as hydrogen bond acceptor or donor at the active site of the receptors and can modulate their activity accordingly. Being polar in nature, the triazole nucleus can increase the solubility of the ligands and contribute better pharmacokinetic and pharmacodynamic properties[8]. In most of the cases, triazole nucleus is found to behave as linker unit with which different functionalities are attached as pharmacophore and at the same time. 1,2,4- triazole ad its derivatives are found to show various biological activity such as antimicrobial, analgesic, anti-inflammatory, anticancer and anti oxidant properties. They are also used as in photosensitive material, as corrosive inhibitors ad in synthesis of various bioactive heterocyclic compounds. Many common medicines available for different disease are found to containing 1,2,4-triazole heterocyclic moiety[9]. 1,2,4-triazole nucleus has received the considerable attention of researchers owing to its wide range of applications in pharmaceuticals, agrochemicals and material sciences[8].

RESEARCH ENVISAGED

Scientists around the world have begun synthesizing and developing a wide range of synthetic antimicrobial agents by the means of organic chemistry. Sulfonamides, nalidixic acid, and quinolones are just few examples of the early synthetic antimicrobial agents with chemotheraptic applications. Recently, triazole compounds such as 1,2,4-triazoles represent an important group of such synthetic antimicrobial compounds that are gaining more interest and access in the field of microbial chemotherapy[10]. More importantly, triazole compounds have clearly shown enormous potential in clinical use as antifungal, anticancer, antibacterial, antitubercular, antiviral, anti-inflammatory, analgesic, anticonvulsant, antiparasitic, antidiabetic, antiobesitic, antihistaminic, anti-neuropathic, antihypertensive, as well as other medicinal drugs. A great deal of effort has been made directly toward the development of triazole-based drugs and numerous excellent achievements have been obtained. Lots of triazole derivatives have been successfully developed, marketed and extensively used in clinic for treatment of various types of diseases with high safety, low toxicity, less adverse effect, high bioavailability, good biocompatibility and drug-targeting, few drug resistances and good curative effects, which have been playing positive roles in bringing benefits to mankind. Particularly excited is that an increasingly number of triazole compounds have been becoming clinical drug candidates in actively ongoing research and development[11].

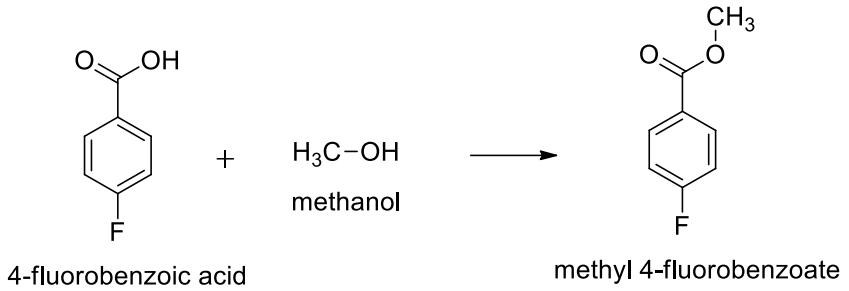
Fungal and bacterial infections have become an important complication and major cause of mortality in immunocompromised individuals suffering from tuberculosis, cancer, AIDS, etc Amphotericin B is the most frequently used drug in the treatment of systemic mycoses in spite of its toxic effect on humans. While various new compounds are often used in treatment of fungal infections, resistance to these drugs is increasing; moreover many of currently available drugs have undesirable side effects, which clearly indicate an urgent need for development of new antimicrobial agents[12,,4].

This study was designed to develop some 1,2,4- triazole derivatives for the purpose of screening its antimicrobial activity against some gram positive and gram negative bacteria,, where the presence of 1,2,4- triazole ring would augment the bioavailability and chemical stability[12].

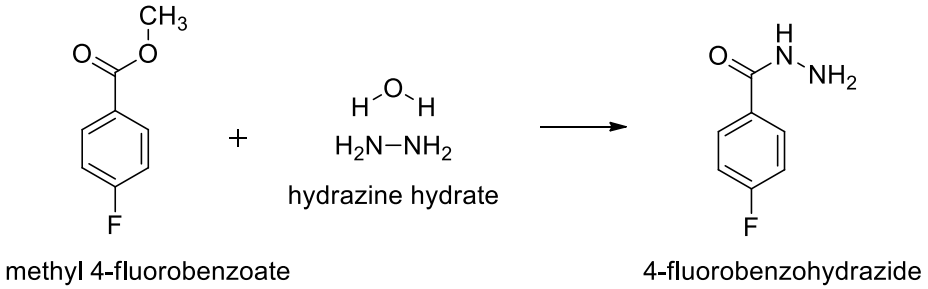
RESEARCH METHODOLOGY

Materials And Methods: Chemical used in the synthesis of title compound described were purchased from chemdyes corporation, sunchem india, oxford laboratory and loba chemie pvt. Ltd. The different substituted compounds for synthesis of proposed derivatives were purchase for online Biomall.in. These chemicals wee used as it is without further purification. All the LR grade reagents were used after purification using the literature method. Melting point were determined by open capillary meltig point apparatus and are uncorrected. For structural characterization of synthesized compound, the IR spectra will recorded in Bruker – 300 MHz spectrometer. ^{1}H NMR spectra were recorded on a Bruker – 500 MHz using tri-methyl sillane as an integral standard. The confirmation of reaction at every step were observe by TLC, using silica gel G (Merck)in a developing solvent system of ethyl acetate ad petroleum ether (1:1) and the spots were visualized with the help of UV chamber and iodine vapors or sulfuric acid (30%v/v) and R_f value were determined . The nitrogen analysis will observe on Perkin Elmer – 2440.

Step-01) Sterification of p- fluorobenzoic acid : p-fluorobenzoic acid will undergo esterification in acidic medium to give an ester (A). 5g (0.035 mol) of 4-fluorobenzoic acid was dissolved in to 3.70 ml (0.091 mol) of methanol in a 100 mL round-bottomed flask. Cautiously, added 3 mL concentrated H2S04 down the side of the flask. After gently swirling the contents of the flask, attached a reflux condenser and reflux the mixture for about 60 min. After completion of the reaction the mixture allowed to cool and transferred the mixture to separating funnel. 50 ml of water was added to the separating funnel and the mixture was washed with the dichloromethane for three times. pH of the solution was adjusted to basic medium. Methyl 4-fluorobenzoate was obtained by evaporating the solvent[13].



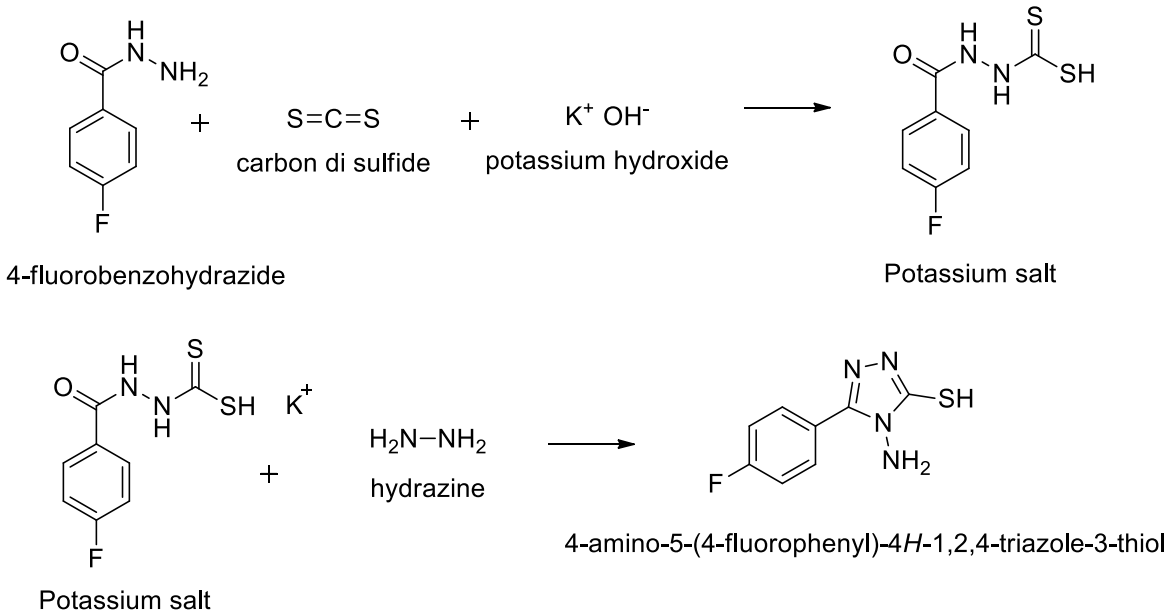
Step-02) The ester with hydrazine hydrate give hydrazide (B): Methyl 4-fluoro benzoate (0.032 mol) and 31.9 ml (0.998 mol) of hydrazine hydrate were mixed in methanol (50 mL). The mixture was refluxed for 6 hours. Methanol was then evaporated and the product formed was being rinsed with plenty of water to remove excess hydrazine hydrate. The product formed was left to dry at room temperature[13].



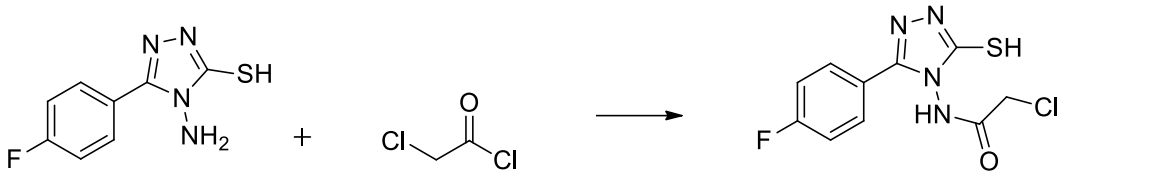
Step-03) Formation of 1-amino-5-(4-fluorophenyl)-3-mercapto-1,2,4-triazole: The hydrazide the reacted with carbon-di-sulphide and potassium salt on stirring for 14-16 hrs(C), which on cyclization with hydrazine will give 1-amino-5-aryl-3-mercapto-1,2,4-triazole (D).

The hydrazide 5gm (0.032 mol) and KOH 1.79 gm (0.032 mol) in 20 Methanol were treated with CS_2 1.92 ml (0.032 mol), and the mixture was stirred for 12–16 h at room temperature. Diethyl ether (20 ml) was added, and the precipitated solid was filtered, washed with ether, and dried. The potassium salts of substituted product were used for the next step without further purification[14].

The potassium salt of the substituted product 5 gm (0.018 mol) and hydrazine hydrate 1.15 ml (0.036 mol) in 2.0 ml water were heated under reflux with stirring for 0.5–1.5 h. Hydrogen sulphide gas was evolved and a homogeneous solution was formed in half an hour. When evolution of hydrogen sulfide ceased, the reaction mixture was diluted with 50 ml cold water and acidified with 6 N hydrochloric acid. The precipitated solid was filtered, washed with cold water[14].



Step-04) Formation of 5-fluorophenyl-4-(chloro-acetyl-amino)-3-mercapto-1,2,4-triazole (E): 4-amino-5-(4-fluorophenyl)-4H-1,2,4-triazole-3-thiol (0.009 mol, 2gm) was mixed with K_2 CO_3 (0.038 mol, 5.25 g) and water (20 ml), and after 5 min, chloroacetyl chloride (0.0135 mol, 1.07 ml) was added drop wise while vigorously stirring. The reaction was stirred for another 30 min at Room temperature and diluted with dichloromethane. Extraction with dichloromethane was followed by washing with water and 1N HCl, drying over Na_2SO_4 and concentrated under reduced pressure[14].



Step-05) Formation of 5-fluoropheyl-4-(sustituted amino)-3-mercapto-1,2,4-triazole: Methanamine (0.0025 mol, 0.77 gm) was mixed with K_2CO_3 (0.0068 mol, 0.939 g) and water (20 ml), and after 5 min, 2-chloro-N-(3-(4-fluorophenyl)-5-mercapto-4H-1,2,4-triazol-4-yl) acetamide (0.0017 mol, 500 mg) was added while vigorously stirring. The reaction was stirred for another 30 min at room temperature and diluted with CH_2Cl_2. Extraction with $CH2Cl_2$ was followed by washing with water and 1N HCl, drying over Na_2SO_4 and concentration under reduced pressure[14].

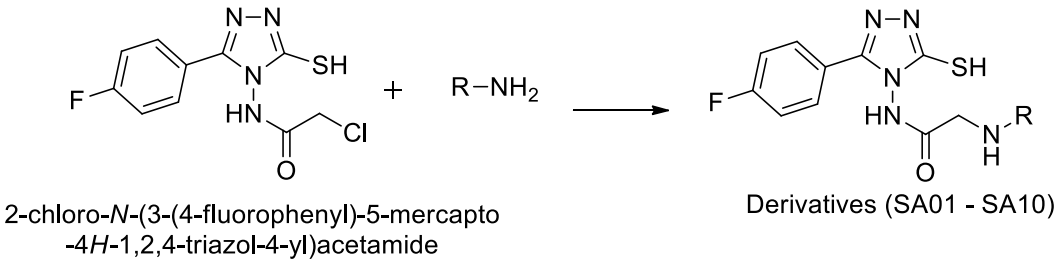
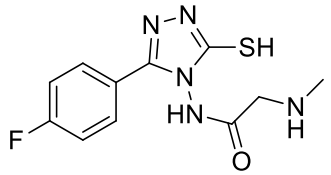
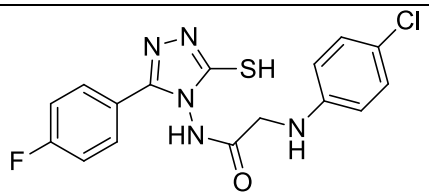


Table 01. Sustituted amines (R) used in synthesis of 1,2,4-Triazole derivatives

S. No	Substituted amines (R)	Proposed Structure	Final triazole Derivatives IUPAC name
1.	Methylamine		N-(3-(4-fluorophenyl)-5-mercapto-4H-1,2,4-triazol-4-yl)-2-(methylamino)acetamide
2.	Chloro-benzyl-amine		2-((4-chlorophenyl)amino)-N-(3-(4-fluorophenyl)-5-mercapto-4H-1,2,4-triazol-4-yl)acetamide

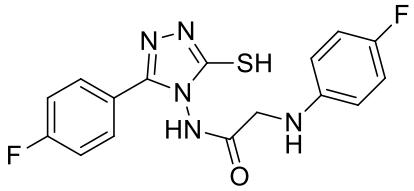
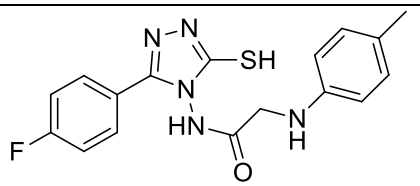
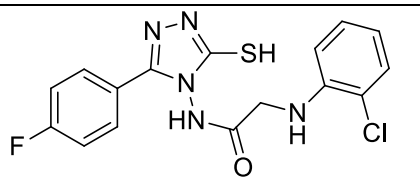
3.	Flouro-benzyl-amine		N-(3-(4-fluorophenyl)-5-mercapto-4H-1,2,4-triazol-4-yl)-2-((4-fluorophenyl)amino)acetamide
4.	Tolyl-amine		N-(3-(4-fluorophenyl)-5-mercapto-4H-1,2,4-triazol-4-yl)-2-(p-tolylamino)acetamide
5.	2-chloro-benzyl-amine		2-((2-chlorophenyl)amino)N-(3-(4-fluorophenyl)-5-mercapto-4H-1,2,4-triazol-4-yl)acetamide

Table 02: Physicochemical data of 5-fluorophenyl-4-(substituted amino)-3-mercapto-1,2,4-triazole. [SA-01 to SA-05]

Compound	R	Molecular weight	Yield (%)	M.P (°C)	R_f Value
SA 01	Methanamine	281.31	35%	220- 222°C	0.63
SA 02	4-chloroaniline	377.82	32%	248-250°C	0.52
SA 03	4- Fluoroaniline	361.37	28%	236-238°C	0.50
SA 04	p-Toluidine	357.41	25%	181-183°C	0.46
SA 05	2-chloroaniline	377.82	32%	200-202°C	0.73

SA-01: N-(3-(4-fluorophenyl)-5-mercapto-4H-1,2,4-triazole-4-yl)-2-(methylamino)acetamide
UV-Visible : λ_{max} is found to be 288.45nm.

FT-IR (KBr cm^{-1}): 3324.53 cm^{-1} (O-H stretching), 3245.96 cm^{-1} (NH stretching), 3100.25 cm^{-1} (CH aromatic) , 2945.16 cm^{-1} (CH stretching alkanes) , 2596.12 cm^{-1} (thiol group), 1745.26 cm^{-1} (carbonyl C=O stretching), 1236.25 cm^{-1} (aromatic CN stretching), 1400.02 cm^{-1} (alkane CH bending).

SA-02 : 2-((4-chlorophenyl)amino)-N-(3-(4-fluorophenyl)-5-mercapto-4H-1,2,4-triazole-4-yl)acetamide
UV-Visible : λ_{max} is found to be 352.64nm.

FT-IR (KBr cm^{-1}) : 3479.24 cm^{-1} (OH stretching), 3389.53 cm^{-1} (NH stretching), 3117.28 cm^{-1} (CH stretching aromatic), 2834.53 cm^{-1} (CH stretching alkane), 2486.29 cm^{-1} (thiol group) , 1689.28 cm^{-1} (carbonyl stretching), 1298.64 cm^{-1} (aromatic CN stretching), 1496.15 cm^{-1} (Alkane CH bending).

SA-03 : N-(3-(4-fluorophenyl)-5-mercapto-4H-1,2,4-triazol-4-yl)-2-((4-fluorophenyl)amino)acetamide
UV-Visible : λ_{max} is found to be 336.73nm.

FT-IR (KBr cm) : 3498.12 cm^{-1} (O–H stretching), 3315.86cm^{-1} (N-H stretching), 3198.15cm^{-1} and 2956.82 cm^{-1}respectively (C-H aromatic and alkane stretching respectively), 2512.34 cm^{-1} (thiol group), 1709.86cm^{-1} (Carbonyl (C=O), 1394.23 cm^{-1} (Aromatic (C–N) stretching), 1483.19 cm^{-1} (Alkane (C–H) bending), 534.39cm^{-1} ((C-Cl) stretching).

^{1}H NMR (500 MHz,CDCL3): δ 3.64 [dd,1H, H of α- carbon of anime group] , δ 4.25 [H of amine group], δ 6.96 [3Hand 5 -H of 4-(fluorophenyl)-5-mercapto-4H-1,2,4-triazole group], δ 7.00- 7.32 [^{1}H , 2H ,3H, 5h ,6H of 4-(fluorophenyl)amino group] , δ7.65 [^{1}H, 2H and 6H of 4-(fluorophenyl)-5-mercapto-4H-1,2,4-triazole group], δ 7.94 [NH of acetamide group].

SA-04 : N-(3-(4-fluorophenyl)-5-mercapto-4H-1,2,4-triazol-4-yl)-2-(p-tolylamino)acetamide
UV-Visible : λ_{max} is found to be 268.57nm.

FT-IR (KBr cm^{-1}): 3425.67 cm^{-1} (O–H stretching), 3383.15 cm^{-1} (N-H stretching), 3289.67 cm^{-1} and 2954.39 cm^{-1} respectively (C-H stretching aromatic and alkane respectively), 2568.36cm^{-1} (thiol group), 1783.62 cm^{-1} (Carbonyl (C=O) stretching), 1353.67 cm^{-1} (Aromatic CN stretching), 1474.33cm^{-1} (Alkane CH bending), 598.23cm^{-1} (C-Cl stretching).

SA-05: 2-((2-chlorophenyl)amino)N-(3-(4-fluorophenyl)-5-mercapto-4H-1,2,4-triazol-4-yl)acetamide
UV-Visible : λ_{max} is found to be 289.58nm.

FT-IR (KBr cm^{-1}): 3474.19 cm^{-1} (alcohol group (OH) stretching) , 3359.26 cm^{-1} (NH stretching), 3286.32cm^{-1} and 2812.36cm^{-1} (C-H stretching aromatic and alkane), 2534.15cm^{-1} (thiol group), 1715.36cm^{-1} (Carbonyl (C=O) stretching), 1324.67cm^{-1}(Aromatic (C–N) stretching), 1432.26cm^{-1} (Alkane (C–H) bending), 533.32cm^{-1} (C-Cl stretching).

Biological Evaluation
Antibacterial Activity:-
The antimicrobial assay of all the synthesized compound was performed by Well Diffusion method. To evaluate the effect of synthesized compound against both gram +ve and gram -ve organism strains representing of each taken. These are *Bacillus Subtilis* and *Pseudomonas aeruginosa.* The fungal strains selected for antifungal screening were *Candida albicans.* Nutrient media used for bacterial strains, stock culture of the microbial strains were prepared from original lyophilized strains using standard method. The nutrient agar media was prepared separately by standard method , and inoculum of 1 gram+ve and 1 gram -ve was prepared , test organism were incubated in 10 ml Nutrient broth. Then , 10 mg of standard (Amoxycillin and Ofloxacin) was taken with 1 ml solvent (distilled water) to make 10mg/10ml solution. The bacterial suspension was standardized to 108 CFU/ml of bacteria and kept into the shaker. Then, 50µl of the inoculum from the broth (containing 108 CFU/ml) was taken with a micropipette and then transferred to fresh and sterile solidified Agar Media Plate (46). The agar plate was inoculated by spreading the inoculum with a sterile spreader, over the entire sterile agar surface. Four wells of 6 mm were bored in the inoculated media with the help of sterile cork-borer. Each well was filled with different concentration (25µg/ml, 50µg/ml, 75µg/ml and 100µg/ml) of sample and another plate well was filled with 50µl of standard drug respectively. It was allowed to diffuse for about 30 minutes at room temperature and incubated for 18-24 hours at 37o C. After incubation, plates were observed for the formation of a clear zone around the well which corresponds to the antimicrobial activity of tested compounds. The zone of inhibition (ZOI) was observed and measured in mm. Zones were measured to a nearest millimeter using a ruler, which was held on the back of the inverted Petri plate. The Petri plate was held a few inches above a black, non-reflecting background. The diameters of the zone of complete inhibition (as judge by unaided eye) were measured, including the diameter of the well and compared to that of conventional compound . All the compounds showed comparable activities as that of standard Ofloxacin (13.5 mm) against *Pseudomonas aeruginosa* .SA -03 [N-(3-(4-fluorophenyl)-5-mercapto-4H-1,2,4-triazol-4-yl)-2-((4-fluorophenyl)amino)acetamide] showed best ZOI (zone of inhibition) of 11.2mm and 12.4mm in diameter at 100µg/ml concentration against gram positive bactertia (*B. Subtilis)* and gram negative bacteria (*Pseudomonas aeruginosa*) which is found to be more prominent to that of standard Ofloxaçin (gram +ve) 13.5mm and Gentamycin (gram -ve) 13.2 mm.[15]

Antibacterial activity of all compounds against gram positive bacteria *Bacillus subtilis*

Compound code	**Different concentrations**			
	25 µg/ml	**50 µg/ml**	**75 µg/ml**	**100 µg/ml**
SA-01	0 mm	0 mm	6.0 mm	8.5 mm
SA-02	0 mm	0 mm	0 mm	8.0 mm
SA-03	0 mm	0 mm	0 mm	11.2 mm
SA-04	0 mm	0 mm	6.5 mm	9.3 mm
SA-05	0 mm	0 mm	6.8 mm	10.8 mm
Ofloxacin	0 mm	0 mm	0 mm	13.5 mm

Table 03: Compound code , Diameter in mm Inhibition.

Antibacterial activity of all compounds against gram negative bacteria *Pseudomonas aeruginosa*

Compound code	**Different concentrations**			
	25 µg/ml	**50 µg/ml**	**75 µg/ml**	**100 µg/ml**
SA-01	0 mm	0mm	6.2 mm	8 mm
SA-02	0 mm	0 mm	6.1 mm	9.6 mm

SA-03	0 mm	0 mm	6.5 mm	12.4 mm
SA-04	0 mm	0 mm	0 mm	10.5 mm
SA-05	0 mm	0 mm	6.1 mm	11.3 mm
Gentamycin	0 mm	0 mm	0 mm	13.2 mm

Table 04: Compound code, Diameter in mm Inhibition.

Antifungal activity if all compounds against *Candida albicans*

Compound code	**Different concentrations**			
	25 µg/ml	**50 µg/ml**	**75 µg/ml**	**100 µg/ml**
SA-01	6.5 mm	6.7 mm	7.4 mm	8.1 mm
SA-02	6.6 mm	6.8 mm	7.3 mm	8.9 mm
SA-03	8.2 mm	8.8 mm	9.8 mm	11.9 mm
SA-04	6.3 mm	6.8 mm	7.4 mm	8.5 mm
SA-05	6.5 mm	6.9 mm	7.4 mm	8.9 mm
Standard (Fluconazole)	7.1mm	8.5 mm	10.2 mm	13.6 mm

Table 05: Compound code , Diameter in mm Inhibition.

RESULTS AND DISCUSSION

The resent study was aimed to synthesized, characterized new 1,2,4 triazole derivatives as antimicrobial agents. All the compounds were prepared by esterification of 4-fluorobenzoic acid and further cyclization of hydrazide. Total five compounds were synthesized and percentage yield were calculated. Characterization of the compounds was performed by TLC and Fourier transforms infrared spectroscopy. Thin layer chromatography of all the synthesized compounds was performed on silica gel plate and n-hexane:ethyl acetate was used as mobile phase, R_f values of all the synthesized compounds were calculated. The amine containing 1,2,4-triazole derivatives were synthesized successfully and their structure were confirmed using FT-IR and ^{1}HNMR. In FT-IR spectra of compounds the characteristic peak of NH stretching , CH aromatic and alkane stretching and carbonyl stretching were observed at 3315.86, 3198.15, 2956.82, and 1709.86 cm^{-1} respectively ,and the compound SA-03 [N-(3-(4-fluorophenyl)-5-mercapto-4H-1,2,4-triazol-4-yl)-2-((4-fluorophenyl)amino)acetamide] OH , Aromatic CN stretching, alkane CH bending ,and C-Cl stretching peak were observed at 3498.12, 1394.23, 1493.19 and 534.39 respectively confirmed the structure of title compounds. . Compounds (SA-01-SA-05) were screened for antibacterial activity against one-gram positive bacteria *Bacillus subtilis* and one gram negative bacteria *Pseudomonas aeruginosa*. The antibacterial activity of all derivatives showed the significant zone of inhibition against *Bacillus subtilis*, and *Pseudomonas aeruginosa*. Thus from the study it is concluded that these new derivatives could serve as effective antimicrobial agents, where SA -03 compound 03 [N-(3-(4-fluorophenyl)-5-mercapto-4H-1,2,4-triazol-4-yl)-2-((4-fluorophenyl)amino)acetamide] have shown their antimicrobial activity less then 12mm against microbial strain. The activity of SA-03 was found to be good activity.

CONCLUSION

As some secondary amines substitutes 1,2,4-triazole containing derivatives compounds were synthesized showed antimicrobial activity , further studies can be performed to evaluate the efficacy and safety of these derivatives .

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